

**EXHIBIT 1
(PART 2 OF 2)**

BAR CODE LABEL



U.S. PATENT APPLICATION

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT
08/487,002	06/07/95	435	1805

APPLICANT

MARK H. SKOLNICK, SALT LAKE CITY, UT; DAVID E. GOLDGAR, SALT LAKE CITY, UT; YOSHIO MIKI, SALT LAKE CITY, UT; JEFF SWENSON, SALT LAKE CITY, UT; ALEXANDER KAMB, SALT LAKE CITY, UT; KEITH D. HARSHMAN, SALT LAKE CITY, UT; DONNA M. SHATTUCK-EIDENS, SALT LAKE CITY, UT; SEAN V. TAVTIGIAN, SALT LAKE CITY, UT; ROGER W. WISEMAN, DURHAM, NC; P. ANDREW FUTREAL, DURHAM, NC.

CONTINUING DATA***

VERIFIED THIS APPLN IS A CIP OF 08/409,305 03/24/95
WHICH IS A CIP OF 08/348,824 11/29/94
WHICH IS A CIP OF 08/308,104 09/16/94
WHICH IS A CIP OF 08/300,266 09/02/94 ABN
WHICH IS A CIP OF 08/289,221 08/12/94

FOREIGN/PCT APPLICATIONS***

VERIFIED

STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS	FILING FEE RECEIVED	ATTORNEY DOCKET NO.
UT	19	28	2	\$1,056.00	24884-109347

TITLE	17Q-LINKED BREAST AND OVARIAN CANCER SUSCEPTIBILITY GENE
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This is to certify that annexed hereto is a true copy from the records of the United States Patent and Trademark Office of the application which is identified above.

By authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS

Date

Certifying Officer

Notice of Allowability	Application No. 08/487,002	Applicant(s) Skolnick et al.
	Examiner Dianne Rees	Group Art Unit 1807

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

This communication is responsive to 2/25/97
 The allowed claim(s) is/are 1-4, 6-8, 10-14, 16-19, and 29-47
 The drawings filed on _____ are acceptable.
 Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 All Some* None of the CERTIFIED copies of the priority documents have been
 received.
 received in Application No. (Series Code/Serial Number) _____
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE **THREE MONTHS** FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

Applicant MUST submit NEW FORMAL DRAWINGS
 because the originally filed drawings were declared by applicant to be informal.
 including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. 10.
 including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.
 including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

Notice of References Cited, PTO-892
 Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
 Notice of Draftsperson's Patent Drawing Review, PTO-948
 Notice of Informal Patent Application, PTO-152
 Interview Summary, PTO-413
 Examiner's Amendment/Comment
 Examiner's Comment Regarding Requirement for Deposit of Biological Material
 Examiner's Statement of Reasons for Allowance

Art Unit: 1807

DETAILED ACTION

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeffrey Inhen on 4/21/97.

2. The application has been amended as follows:

Claim 48 has been canceled.

The following is an examiner's statement of reasons for allowance:

The claims are drawn to methods of screening a tumor sample for a somatic alteration in a BRCA1 gene by detecting changes in the structure and/or expression of the gene and its products (transcripts and proteins expressed by said transcripts). In a further embodiment of the invention, the detection of specific mutant alleles is recited. Applicants are first to discover the sequence of the wild type BRCA1 gene and disclose and enable the methods of detection recited broadly herein (Applicant's declaration by Dr. Wolfert was considered persuasive with regards to method

claims employing altered -epitope specific antibodies. The skill in the art in this technology is high and such antibodies have been routinely made for a number of years. It is further noted that workers in the field have generated antibodies to various domains of the BRCA1 protein subsequent to the filing of this application using the same methodology disclosed in the instant application). Detection of somatic alterations are an indication of a progression to neoplasia when such alterations are opposite a chromosome comprising a germline alteration in the BRCA1 gene and thus the present invention provides a useful screening to assess progression to neoplasia in patients with breast or ovarian cancer.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dianne Rees whose telephone number is (703) 308-6565.

Dianne Rees
4/28/97

W. GARY JONES
SUPERVISORY PATENT EXAMINER
GROUP 1800
5/12/97

5753441

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PATENT
SERIAL
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MAY 9 1996PATENT
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SERIAL NUMBER

FILING DATE

CLASS

435

SUBCLASS

6

GROUP ART UNIT

?

EXAMINER

Rees

APPLICANT: MARK H. SKOLNICK, SALT LAKE CITY, UT; DAVID E. GOLDMAN, SALT LAKE CITY, UT; YOSHIO MIKI, SALT LAKE CITY, UT; JEFF GLENNON, SALT LAKE CITY, UT; ALEXANDER KANB, SALT LAKE CITY, UT; KEITH D. HARSHMAN, SALT LAKE CITY, UT; MONNA M. SHATTUCK-SEIDEN, SALT LAKE CITY, UT; SEAN V. TAVTIGIAN, SALT LAKE CITY, UT; ROGER W. WISEMAN, DURHAM, NC; P. ANDREW FUTREAU, DURHAM, NC.

CONTINUING DATA*

VERIFIED THIS APPN IS A CIP OF 09/409,306 09/24/95
 WHICH IS A CIP OF 08/348,824 11/29/94
 /DR S/1797 WHICH IS A CIP OF 08/308,104 09/16/94
 WHICH IS A CIP OF 08/300,266 09/02/94 AEN
 WHICH IS A CIP OF 08/289,291 08/12/94

Rees 435/6

FOREIGN/PCT APPLICATIONS*

VERIFIED

NONE DR S/1797

NOTE DISCLAIMER

The term of this patent shall not extend beyond the expiration date of Pat. No. 5710001

FOREIGN FILING/LICENSE GRANTED 04/05/96

Foreign priority claimed 35 USC 119 conditions met	<input type="checkbox"/> yes <input checked="" type="checkbox"/> no	AS FILED	STATE OR COUNTRY	Sheets Drawgs.	TOTAL CLAIMS	INDEP. CLAIMS	FILING FEE RECEIVED	ATTORNEY'S DOCKET NO.
Verified and Acknowledged	<input checked="" type="checkbox"/> yes <input type="checkbox"/> no	Examiner's Initials	US	19	27	2	\$11,034.00	24082-10

ADDRESS
 VENABLE BAETJER HOWARD AND CO., LLP
 1201 NEW YORK AVENUE NW
 SUITE 1000
 WASHINGTON DC 20005

17q-LINKED BREAST AND OVARIAN CANCER SUSCEPTIBILITY REGION

U.S. DEPT. OF COMM/PAT. & TM PTO-436 Rev.12

PARTS OF APPLICATION PRINT SEPARATELY		DIANNE REES Assistant Examiner	
NOTICE OF ALLOWANCE MAILED		CLAIMS ALLOWED	
ISSUE FEE		Total Claims 37	
APPLICANT DUE DATE PAID		Print Claim 1	
18/19/96		DRAWING	
SHEETS DRAWGS 18/19/96		Sheets Drawgs 18/19/96	
ISSUE BATCH NUMBER		Print Fld 1	
1028		1028	
PREPARED FOR ISSUE			
WARNING: The information disclosed herein may be restricted. Unauthorized disclosure may be prohibited by the United States Code, Title 35, Sections 122, 181 and 368. Possession outside the U.S. Patent & Trademark Office is restricted to authorized employees and contractors only.			

ISSUE FEE IN FILE

(FACE)

SEARCHED

Class	Sub.	Date	Exmr.
435	6	7/1/96	DR
435	91,1		
435	91,2		
435	7,1-7,9		
536	23,1		
536	24,3 38		
updated search			
updated search			
added 436			
435 4			
424 1,11			
436 548			
536 387,2			
530 388,11			
424 388,11			

SEARCH NOTES

	Date	Exmr.
APS, STN-see Search notes in related cases, Seq ID's updated search	7/1/96	DR
updated search talked to A, Atzel	4/12/97	DR
updated search	5/18/97	DR

INTERFERENCE SEARCHED

Class	Sub.	Date	Exmr.
435	6	5/18/97	DR
	91,1, 91,2		
	7,1-7,9		
436	4		
	548		
	300		
530	387,2		
	386,1		
424	1,11, 88		
536	23,1		
	24,3		
	24,33		
Seq	019		

(RIGHT OUTSIDE)

POSITION	ID NO.	DATE
CLASSIFIER		
EXAMINER	401	8-17-95
TYPIST	4013	4/5/96
VERIFIER		
CORPS CORR.		
SPEC. HAND	455	1-5-96
FILE MAINT.	457	8-17-95
DRAFTING		

INDEX OF CLAIMS

Claim	Original	Date
1	1	7/26/92
2	2	1-15-93
3	3	1-15-93
4	4	1-15-93
5	5	11-11
6	6	11-11
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8	8	✓ 11
9	9	11-11
10	10	11-11
11	11	11-11
12	12	11-11
13	13	✓ 11
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32	32	✓
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40	40	✓
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46	46	11-11
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48	48	✓ 11
49	49	
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SYMBOLS

✓	Rejected
-	Allowed
- (Through number)	Cancelled
+	Restricted
N	Non-elected
I	Interference
A	Appeal
O	Objected

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Notice of Allowability	Application No. 08/488,011	Applicant(s) Skolnick et al.	Examiner Dianne Rees	Group Art Unit 1807	

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

This communication is responsive to 9/12/96, 4/30/97.

The allowed claim(s) is/are 1-4, 6-8, 10-13, 13, 14, 14-19, and 28-48.

The drawings filed on _____ are acceptable.

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

Applicant MUST submit NEW FORMAL DRAWINGS

because the originally filed drawings were declared by applicant to be informal.

including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. 7.

including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.

including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 9, 10

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

Interview Summary, PTO-413

Examiner's Amendment/Comment

Examiner's Comment Regarding Requirement for Deposit of Biological Material

Examiner's Statement of Reasons for Allowance

DETAILED ACTION

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeffrey Inhen on May 19, 1997

The application has been amended as follows:

In claims 41-47, the words "comprises the alteration comprising" has been deleted and --
consists of-- has been inserted.

3. The following is an examiner's statement of reasons for allowance:

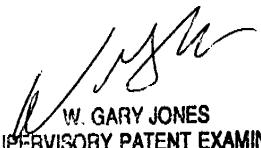
The claims are drawn to methods of detecting germline alterations in the BRCA1 gene by detecting alterations in BRCA1 nucleic acids or in the products expressed by these nucleic acids, such as by the use of epitope specific antibodies. In a further embodiment of the invention, the method is used to detect specific polymorphisms in the BRCA1 gene. Applicants are first to discover the sequence of the wild type BRCA1 gene and disclose and enable the methods of detection recited broadly herein (Applicant's declaration by Dr. Wolfert was considered persuasive with regards to method claims employing altered -epitope specific antibodies). The skill in the art in this technology is high and such antibodies have been routinely made for a number of years. It is further noted that workers in the field have generated antibodies to various domains of the BRCA1 protein subsequent to the filing of this application using the same methodology disclosed in the instant application. Detection of germline mutations in the BRCA1 gene provide an indication of increased susceptibility to breast and ovarian cancer.

Art Unit: 1807

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dianne Rees whose telephone number is (703) 308-6565.

Dianne Rees
5/19/97

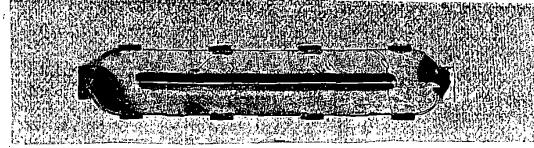

W. GARY JONES
SUPERVISORY PATENT EXAMINER
GROUP 1800

5/19/97

May 19, 1997

jc525 U.S. PTO
09/044946
03/28/98


435	6
Class	Subclass
ISSUE CLASSIFICATION	



PATENT NUMBER
6033857

6033857

U.S. UTILITY PATENT APPLICATION

SCANNED <i>SM</i>	O.I.P.E. <i>SC</i>	PATENT DATE <i>MAY 07 1999</i>
Q.A. <i>SW</i>		

SECTOR	CLASS 435	SUBCLASS 6	ART UNIT 1632	EXAMINER Hauda
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FILED WITH: DISK (CRF) FICHE
(Attached in pocket on right inside flap)

PREPARED AND APPROVED FOR ISSUE

ISSUING CLASSIFICATION

ORIGINAL		CROSS REFERENCE(S)			
CLASS	SUBCLASS	CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)		
435	6	435	7.2	69.1	325 320.1
INTERNATIONAL CLASSIFICATION		536	23.1	23.5	
C07H	21/00				
C12N	15/63				
C12N	15/79				
C12N	15/11				
C12N	15/09				

Continued on Issue Slip Inside File Jacket

TERMINAL DISCLAIMER	DRAWINGS			CLAIMS ALLOWED	
	Sheets Drwg.	Figs. Drwg.	Print Fig.	Total Claims	Print Claim for O.G.
	9	11	NONE	8	1
<input type="checkbox"/> a) The term of this patent subsequent to _____ (date), has been disclaimed.				NOTICE OF ALLOWANCE MAILED	
<input type="checkbox"/> b) The term of this patent shall not extend beyond the expiration date of U.S Patent. No. _____	<i>Karen M. Hauda 9/29/99</i>			<i>10-1-99</i>	
	<i>Karen M. Hauda</i>			ISSUE FEE <i>100</i>	
	<i>Primary Examiner</i>			Amount Due	Date Paid
<input type="checkbox"/> c) The terminal _____ months of this patent have been disclaimed.	<i>(Legal Instruments Examiner)</i>			<i>100500</i>	<i>12-21-99</i>
ISSUE BATCH NUMBER <i>C62</i>					

WARNING:

The information disclosed herein may be restricted. Unauthorized disclosure may be prohibited by the United States Code Title 35, Sections 122, 181 and 368. Possession outside the U.S. Patent & Trademark Office is restricted to authorized employees and contractors only.

Form PTO-436A
(Rev. 10/97)

Formal Drawings (*9* sheets set)

(LABEL AREA)

(FACE)

PATENT APPLICATION



09044946

MAR 30 19835
INITIALS

CONTENTS

Date received
(Incl. C. of M.)
or

Date Mailed

Date received
(Incl. C. of M.)
or

Date Mailed

1. Application papers 4/16/98
 2. Notice Re Insufficiency 42.
 3. Response 6/10/98
 4. Patent mailed 3-20-98
 5. SIDS 3-20-98
 6. Status Report 6-1-99
 7. CPR 7/1/99
 8. 2nd Th. 89 9/25/99
 9. CRF entered 9/30/99
 10. Notice of Allowance/Ex. Comm. 10/1/99
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SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY D
09/044,946	03/20/98	800	1632	2318-18

APPLICANT SEAN V. TAVTIGIAN, SALT LAKE CITY, UT; ALEXANDER KAMB, SALT LAKE CITY, UT; JACQUES SIMARD, QUEBEC, CANADA; FERGUS COUCH, ST DAVIDS, PA; JOHANNA M. ROMMENS, TORONTO ONTARIO, CANADA; BARBARA L. WEBER, MERION, PA.

CONTINUING DOMESTIC DATA***

VERIFIED THIS APPLN IS A DIV OF 08/639,501 04/29/96 PAT 5,837,4
KM/H WHICH IS A CIP OF 08/585,391 01/11/96 ABN
 WHICH IS A CIP OF 08/576,559 12/21/95 ABN
 WHICH IS A CIP OF 08/573,359 12/20/95 ABN
 WHICH IS A CIP OF 08/573,779 12/18/95 ABN

371 (NAT'L STAGE) DATA***

VERIFIED

KM/H *None*

FOREIGN APPLICATIONS***

VERIFIED

KM/H *None*

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 04/07/98 ** SMALL ENTITY **

Foreign Priority claimed 35 USC 119 (a-d) conditions met	<input type="checkbox"/> yes <input checked="" type="checkbox"/> no <input type="checkbox"/> Met after Allowance	STATE OR COUNTRY UT	SHEETS DRAWING 9	TOTAL CLAIMS 13	IN CL
Verified and Acknowledged Examiner's Initials	<u>KM/H</u>	Initials			

ADDRESS	JEFFREY L IHNNEN ROTHWELL FIGG ERNST & KURZ SUITE 701-EAST 555 13TH STREET NW WASHINGTON DC 20004
TITLE	CHROMOSOME 13-LINKED BREAST CANCER SUSCEPTIBILITY GENE

FILING FEE RECEIVED \$477	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT NO. _____ for the following:	<input type="checkbox"/> All Fees <input type="checkbox"/> 1.16 Fees (Filing) <input type="checkbox"/> 1.17 Fees (Processing Ext. of <input type="checkbox"/> 1.18 Fees (Issue) <input type="checkbox"/> Other _____
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Notice of Allowability	Application No.	Applicant(s)
	09/044,946	Tavtigian et al.
Examiner	Group Art Unit	
Karen M. Hauda	1632	

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course.

This communication is responsive to March 20, 1998

The allowed claim(s) is/are 35, 49, 51, 52, 55, and 57-59

The drawings filed on Mar 20, 1998 are acceptable.

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

A SHORTENED STATUTORY PERIOD FOR RESPONSE to comply with the requirements noted below is set to EXPIRE THREE MONTHS FROM THE "DATE MAILED" of this Office action. Failure to timely comply will result in ABANDONMENT of this application. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION, PTO-152, which discloses that the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.

Applicant MUST submit NEW FORMAL DRAWINGS

because the originally filed drawings were declared by applicant to be informal.

including changes required by the Notice of Draftsperson's Patent Drawing Review, PTO-948, attached hereto or to Paper No. _____.

including changes required by the proposed drawing correction filed on _____, which has been approved by the examiner.

including changes required by the attached Examiner's Amendment/Comment.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the reverse side of the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any response to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE/SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

Interview Summary, PTO-413

Examiner's Amendment/Comment

Examiner's Comment Regarding Requirement for Deposit of Biological Material

Examiner's Statement of Reasons for Allowance

Karen M. Hauda
Karen M. Hauda
Patent Examiner

Application/Control Number: 09/044,946

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EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Jeffrey L. Ihnen on September 28, 1999.

The application has been amended as follows:

Claim 49 has been rewritten as follows:

Claim 49. A method for diagnosing a predisposition for breast cancer in a human subject which comprises comparing the germline sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from said subject with the germline sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the germline sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a predisposition to said cancer.

Claim 50 has been canceled.

In claim 51, line 1, the term "the" has been replaced with the term "a".

In claim 51, line 1, the term "regions" has been replaced with the term "region".

In claim 52, line 1, the phrase "determined by an assay" has been inserted after the word "is".

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In claim 52, line 4, the term “sample” has been inserted after the term “tissue”.

In claim 52, line 5, the phrase “of the tissue ~~sample~~” has been inserted after the term “DNA”.

In claim 52, line 5, the phrase “tissue” has been ~~been inserted~~ after the term “said”.

In claim 52, line 7, the phrase “from said tissue sample using primers” has been inserted after the term “gene”.

In claim 52, line 8, the term “tissue” has been ~~been inserted~~ before the term “sample”.

In claim 52, line 9, the term “molecules” has been ~~been deleted~~.

In claim 52, line 9, the phrase “BRCA2 gene/genomic DNA or” has been replaced with the phrase “a BRCA2 gene or a”..

In claim 52, line 10, the term “tissue” has been inserted before the term “sample”.

In claim 52, line 11, the term “DNA” has been replaced with the term “sequence”.

In claim 52, line 12, the term “tissue” has been inserted before the term “sample”.

In claim 52, line 14, the term “sample” has been inserted after the term “tissue”.

In claim 52, line 16, the phrase “in said tissue sample” has been inserted after the term “mutation”.

In claim 52, line 17, the phrase “in said tissue sample” has been inserted after both occurrences of the term “mutation”.

In claim 52, line 17, the “.” after the first occurrence of the term mutation has been replaced with a “,”.

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In claim 52, line 18, the phrase "of said tissue sample" has been inserted after the first occurrence of the term "gene".

In claim 52, line 18, from the comma after the second occurrence of the term "gene" to the end of the claim excluding the period has been deleted.

Claims 53-54 have been canceled.

Claim 55 has been rewritten as follows:

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Claim 55. A method for detecting a mutation in a neoplastic lesion at the BRCA2 gene in a human subject which comprises comparing the sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from a lesion of said subject with the sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein an alteration in the sequence of the BRCA2 gene or the sequence of its mRNA of the subject indicates a mutation at the BRCA2 gene of the neoplastic lesion.

Claim 56 has been canceled.

In claim 57, line 1, the term "a" has been inserted before the term "regulatory".

In claim 58, line 1, the phrase "determined by an assay" has been inserted after the word "is".

In claim 58, line 4, the term "sample" has been inserted after the term "tissue".

In claim 58, line 4, the phrase "of the tissue sample" has been inserted after the term "DNA".

In claim 58, line 5, the phrase "tissue" has been inserted after the term "said".

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In claim 58, line 7, the phrase “from said tissue sample using primers” has been inserted after the term “gene”.

In claim 58, line 8, the term “tissue” has been inserted before the term “sample”.

In claim 58, line 9, the term “molecules” has been deleted.

In claim 58, line 9, the phrase “BRCA2 gene genomic DNA or” has been replaced with the phrase “a BRCA2 gene or a”.

In claim 58, line 10, the term “tissue” has been inserted before the term “sample”.

In claim 58, line 11, the term “DNA” has been replaced with the term “sequence”.

In claim 58, line 12, the term “tissue” has been inserted before the term “sample”.

In claim 58, line 14, the term “sample” has been inserted after the term “tissue”.

In claim 58, line 16, the phrase “in said tissue sample” has been inserted after both occurrences of the term “mutation”.

In claim 58, line 17, the “.” after the second occurrence of the term mutation has been replaced with a “,”.

In claim 58, line 17, the phrase “in said tissue sample” has been inserted after the term “mutation”.

In claim 58, line 17, the phrase “of said tissue sample” has been inserted after the term “gene”.

In claim 58, line 18, from the comma after the term “gene” to the end of the claim excluding the period has been deleted.

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Claim 59 has been rewritten as follows:

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Claim 59. A method for confirming the lack of a BRCA2 mutation in a neoplastic lesion from a human subject which comprises comparing the sequence of the BRCA2 gene or the sequence of its mRNA in a tissue sample from a lesion of said subject with the sequence of the wild-type BRCA2 gene or the sequence of its mRNA, wherein the presence of the wild-type sequence in the tissue sample indicates the lack of a mutation at the BRCA2 gene.

Claim 60 has been canceled.

The following is an examiner's statement of reasons for allowance:

The claimed invention is allowable over the prior art of record because the prior art of record does not teach or fairly suggest a method of screening for a mutation in a sample by comparing the DNA gene sequence of BRCA2 from the sample with that of the wild-type BRCA2 gene sequence.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen M. Hauda whose telephone number is (703) 305-6608.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, may be reached at (703) 308-4743.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-2801.

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**The Group and/or Art Unit location of your application in the PTO has changed.
To aid in correlating any papers for this application, all further correspondence regarding
this application should be directed to Group Art Unit 1632.**

Papers related to this application may be submitted to Group 160 by facsimile transmission. Papers should be faxed to Group 160 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is or (703) 305-3014 or (703) 308-4242.

Karen M. Hauda
Karen M. Hauda
Patent Examiner